

addition of claims) are hereby authorized to be charged to our Deposit Account No.

19-0036.

Amendments

In the Specification:

Please ~~insert~~ the attached, independently numbered Sequence Listing at the end of the application.

Please ~~substitute~~ the 1st full paragraph on page 1, with the following paragraph:

This is a divisional of U.S. Patent Application Serial No. 09/220,077, filed December 23, 1998, which claims the benefit, under 35 U.S.C. § 119(e), of the earlier filing date of U.S. Provisional Application, Appl. No. 60/068,667, filed on December 23, 1997. The entirety of each of these applications is incorporated by reference herein.

Please ~~substitute~~ the 3rd full paragraph on page 6, with the following paragraph:

Figure 1. This figure presents the DNA (SEQ ID NO:1) and amino acid (SEQ ID NO:2) sequence of the 157 amino acid form of bFGF used in this invention. The N-terminal, initiating methionine is processed by *E. coli*, and the purified bFGFs, therefore, lack the first amino acid shown in the figure. The nucleic acid sequence reported in this

A2
concl.

[illegible]

A3

Please substitute the paragraph beginning on page 28, line 18, with the following paragraph:

All other mutations reported in Table 1 were constructed using cassette mutagenesis.

The L137A mutation was made by inserting complementary oligonucleotides into the AflII and ApaI sites in which the CTT codon for leucine was replaced with the GCT codon for alanine (Figure 1). A HindIII site (not shown) was removed for convenient screening of positives. The DNA sequence for the above mentioned mutations differs somewhat from that which appears in Figure 1 although the amino acid sequence remains identical except for the introduced site-directed mutations. The DNA sequence for the E89A, E89Y, D101A and L137A mutants differs from that reported in Figure 1 only between the KpnI and ApaI restriction enzyme sites. Except for the introduced mutation (boxed codon in Figure 1) the following DNA sequence between the KpnI and ApaI sites is representative for the E89A, E89Y, D101A and L137A mutants:

CTGGCTATGAAGGAAGATGGAAGATTACTGGCTTCTAAATGTGTTACGGATG
AGTGTTTCTTTTTTGAACGATTGGAATCTAATACTACAATACTTACCGCTCG
AGAAAATACACCAGTTGGTATGTGGCACTTAAGCGTACCGGTCAGTACAAGC
TTGGTTCTAAAACGGGCC (SEQ ID NO:3). The E89A and D101A double mutation reported in Table I was constructed by inserting complementary oligonucleotides into the KpnI and XhoI sites (Figure 1). The E89A, D101A, L137A triple mutant was constructed by combining the E89A, D101A double mutant with the single L137A mutant using the restriction enzyme sites engineered into the DNA sequence (Figure 1). All mutations were confirmed by DNA sequencing of plasmid DNA. Cassette mutagenesis was performed using the bFGF expression construct (see below) such that no further subcloning was required.